View metadata, citation and similar papers at core.ac.uk

brought to you by CORE

provided by Elsevier - Publisher Connector

coronary artery in patients with acute myocardial infarction. J Am Coll Cardiol 2007;50:1305–9.
2. Joner M, Finn AV, Farb A, et al. Pathology of drug-eluting stents in humans: delayed healing and late thrombotic risk. J Am Coll Cardiol 2006;48:193–202.
3. Togni M, Windecker S, Cocchia R, et al. Sirolimus-eluting stents associated with paradoxic coronary vasoconstriction. J Am Coll Cardiol 2005;46:231–6.
4. Finn AV, Nakazawa G, Joner M, et al. Vascular responses to drug eluting stents: importance of delayed healing. Arterioscler Thromb Vasc Biol 2007;27:1500–10.
5. Wysocki SJ, Zheng MH, Smith A, Norman PE. Vascular endothelial growth factor (VEGF) expression during arterial repair in the pig. Eur J Vasc Endovasc Surg 1998;15:225–30.

Reply

We appreciate the opportunity to reply to questions raised by Dr. Nakazawa and colleagues. Please note that the coronary arteries distal to the stented segment but not the stented lesion were examined for the endothelial vasomotor function in our study (1). As described in our study (1), myocardial ischemia-reperfusion induces endothelial injury in the coronary trees for their entirety distal to the occluded segment in the infarct-related coronary artery. Thus, the healing process of the coronary arteries distal to the stented segment but not the stented lesion affected our data. Our previous reports (2–5) agreed that the atherosclerotic burden strongly affects coronary endothelial vasomotor functions. However, our study (1) showed that the frequencies of the atherosclerotic risk factors were comparable between the drug-eluting stent (DES) and bare-metal stent (BMS) groups. In addition, the 2 groups had no difference in cardiac medications, lesion, and procedural variables of percutaneous coronary intervention except for stent selection, and acute myocardial infarction (AMI)–related variables that potentially influence the coronary endothelial vasomotor function, as described in our study (1). Thus, the implanted stents were only the discriminate factor for the difference in the coronary endothelial vasomotor responses to acetylcholine between the patients treated with BMS and DES.

A number of previous reports (6,7) demonstrated that the vascular endothelial growth factor (VEGF) expression is increased in cardiomyocytes as well as vascular endothelial cells in ischemic or injured hearts and that sirolimus is capable of inhibiting VEGF production and the VEGF-mediated cellular signaling pathway in various types of cells. Our study (1) also showed that VEGF levels in the anterior interventricular vein (AIV), reflecting VEGF levels released from the ischemic myocardium, were increased in AMI patients treated with BMS compared with control subjects. As we described in our study (1), sirolimus levels in AIV in our study were 10- to 500-fold lower than the levels to exert its biological effects in vitro experiments (8,9). Considering the fact that sirolimus is eluted into coronary circulation over a period of 4 weeks, these exposure times were much longer as compared with the in vitro experiments. Moreover, the chronic exposure to the circulating sirolimus might cause a local accumulation of considerable amounts of this drug in the myocardium and the entire vascular bed distal to sirolimus-eluting stent (SES) in the infarct-related coronary artery. Thus, there is a possibility that SES could induce a decrease in VEGF release from myocardium and endothelium of large and resistance vessels, which may play a possible role in the mechanisms for endothelial vasomotor dysfunction in the infarct-related coronary arteries treated with SES.

Jyun-ei Obata, MD, PhD
***Kiyotaka Kugiyama, MD, PhD**

*Department of Internal Medicine II
Interdisciplinary Graduate School of Medicine and Engineering
University of Yamanashi
1110 Shimokato
Chuo City, Yamanashi Prefecture, 409-3898
Japan
E-mail: kugiyama@yamanashi.ac.jp

doi:10.1016/j.jacc.2007.12.007

REFERENCES

1. Obata JE, Kitta Y, Takano H, et al. Sirolimus-eluting stent implantation aggravates endothelial vasomotor dysfunction in the infarct-related coronary artery in patients with acute anterior myocardial infarction. J Am Coll Cardiol 2007;50:1305–9.
2. Kugiyama K, Kerns SA, Morrisett JD, Roberts R, Henry PD. Impairment of endothelium-dependent arterial relaxation by lysolecithin in modified low-density lipoproteins. Nature 1990;344:160–2.
3. Kugiyama K, Yasue H, Ohgushi M, et al. Deficiency in nitric oxide bioactivity in epicardial coronary arteries of cigarette smokers. J Am Coll Cardiol 1996;28:1161–7.
4. Kugiyama K, Doi H, Motoyama T, Soejima H, et al. Association of remnant lipoprotein levels with impairment of endothelium-dependent vasomotor function in human coronary arteries. Circulation 1998;97:2519–26.
5. Kawano H, Motoyama T, Kugiyama K, et al. Hyperglycemia rapidly suppresses flow-mediated endothelium-dependent vasodilation of brachial artery. J Am Coll Cardiol 1999;34:146–54.
6. Hojo Y, Ikeda U, Zhu Y, et al. Expression of vascular endothelial growth factor in patients with acute myocardial infarction. J Am Coll Cardiol 2000;35:968–73.
7. Lee SH, Wolf PL, Escudero R, Deutsch R, Jamieson SW, Thistlethwaite PA. Early expression of angiogenesis factors in acute myocardial ischemia and infarction. N Engl J Med 2000;342:626–33.
8. Guba M, von Breitenbuch P, Steinbauer M, et al. Rapamycin inhibits primary and metastatic tumor growth by antiangiogenesis: involvement of vascular endothelial growth factor. Nat Med 2002;8:128–35.
9. Dichtl W, Stocker EM, Mistlberger K, et al. Countervailing effects of rapamycin (sirolimus) on nuclear factor-κB activities in neointimal and medial smooth muscle cells. Atherosclerosis 2006;186:321–30.

Early Detection of Rheumatic Heart Disease and Prevention of Heart Failure in Sub-Saharan Africa

In a recent issue of the *Journal*, Damasceno et al. (1) highlighted the need for action to reduce the prevalence of heart failure in sub-Saharan Africa, where this pathology is an important cause of mortality as well as a serious economic burden. Rheumatic heart disease is the most frequent cause of heart failure in this region of the world and is responsible for at least one-third of cases. In this context, the authors are prudent to insist on the need for a strategy of prevention with regards to risk factors for heart failure. Nevertheless, we would like to underline important new findings that should be considered when attempting to reduce the incidence of this life-threatening pathology.